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UNIVERSITY OF VIRGINIA PATENT FOUNDATION
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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,805	GUERRANT ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *8,18 and 23-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-17 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final rejection filed on January 23, 2008 is acknowledged. Claims 1-30 are pending in this application. Applicant elected Group I (claims 1-23, 25 and 26) and elected species ALA(GLN)n for the amino acid sequence, nelfinavir for the antiretroviral drug, and trypsin for the protease cleavage site in reply filed on June 22, 2007. Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, thus, the election had been treated as an election without traverse. Claims 8, 18 and 23-30 remain withdrawn from further consideration as being drawn to nonelected species and invention. Applicant requested reconsideration of withdrawal of claims 8, 18 and 30. However, Applicant elected species ALA(GLN)n without distinctly and specifically pointing out the supposed errors. A search for Ala(Gln)n (e.g., Ala-Gln-Gln-Gln-Gln) would not lead to Met(ALA-GLN)n, MET(ALA-GLN-GLN)n or Met[(ALA-GLN)n-protease cleavage site-(ALA-GLN)p]m (e.g., Met-Ala-Gln-Ala-Gln-Ala-Gln-Ala-Gln). Therefore, the withdrawal of claims 8, 18 and 30 are maintained. Claims 1-7, 9-17 and 19-22 are examined on the merits in this office action.

Withdrawn Objection

1. Objection to the title is hereby withdrawn due to Applicant's arguments

2. Rejection under 35 U.S.C. 103(a) is hereby withdrawn due to Applicant's arguments.

Maintained Rejections

35 U.S.C. 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3-7, 9-11, 13-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Guerrant et al (US Patent # 5561111) as evidenced by the British Pharmaceutical Codex (see www.henriettesherbal.com/eclectic/bpc1911/glucosum.html).

5. The instant claims are drawn to a method of enhancing the absorption of a pharmaceutical agent administered orally to a mammal, the method comprising the steps of administering to the mammal a composition comprising a glutamine-bearing compound ($Ala(Gln)_n$), and administering orally to the mammal the pharmaceutical agent, wherein the mammal is a human subject having compromised intestinal function.

6. Guerrant et al teach a method for the treatment of dehydration or nitrogen deficiency-based malnutrition involving administering to a patient in need thereof an effective amount of a compound selected from oligopeptides formed from the coupling of one or more amino acid with glutamine, the product of coupling glucose with glutamine, the product of coupling glucose and one or more amino acids with glutamine, or the product from acylating glutamine with a carboxylic acid having from 2 to 6 carbon atoms (see abstract). This reads on claims 1, 3-5, 11 and 13-15, since glucose can be

used as a pharmaceutical agent as a restorative agent after severe operation or as a nutritive in wasting diseases, as evidenced by the British Pharmaceutical Codex (see www.henriettesherbal.com/eclectic/bpc1911/glucosum.html). Furthermore, the reference teaches that glutamine derivatives effectively block the degradation of glutamine in the highly acidic conditions, which are encountered in the human stomach. In order to perform effectively in oral therapy, the compounds must be able to survive the conditions in the digestive tract while maintaining the ability to stimulate their absorption and maintain the integrity of the intestinal mucosa (see column 4, lines 12-18). Furthermore, the reference teaches that the glutamine derivatives can be administered either orally or intravenously (see column 4, lines 24-25). This reads on claim 4. Additionally, the reference teaches that the glutamine-bearing compound is Ala-Gln (see Example and Figure 1). This reads on claims 6, 7, 9-10, 16-17 and 19. Thus, the prior reads on claims 1, 3-7, 9-11, 13-17 and 19. Please note that the intended use has not been given any patentable weight, since they do not further limit the compound.

Response to Applicant's Arguments

7. Applicant argues that "Guerrant does not teach, or even contemplate, enhancing absorption of a pharmaceutical agent using glutamine as recited in the present application. Guerrant only teaches methods of delivering glutamine itself, by modifying glutamine for the "treatment of dehydration or nitrogen deficiency-based malnutrition." Furthermore, Applicant argues that "the present application teaches and claims using glutamine to enhance absorption of other compounds, not enhancing absorption of

glutamine itself." Furthermore, Applicant argues that "regarding the Examiner's assertion that glucose is a pharmaceutical agent, it was overlooked by the Examiner that the glucose of Guerrant must be coupled to the glutamine and that the glucose is coupled to the glutamine to form a compound which is less susceptible to degradation….the data only addresses absorption of the glutamine derivatives Ala-Glu and Ala-Gln and shows that Gln alone degrades faster under increasingly acidic conditions. Nowhere does Guerrant teach or suggest that a glutamine derivative can enhance the absorption of a pharmaceutical agent."

8. Applicant's arguments have been fully considered but have not been found persuasive because Guerrant et al teach a method of treating malnutrition involving administration to a patient in need thereof an effective amount of a compound selected from oligopeptides formed from the coupling of one or more amino acid with glutamine, the product of coupling glucose with glutamine, the product of coupling glucose and one or more amino acid with glutamine, or the product from acylating glutamine with a carboxylic acid. The compounds, such as oligopeptides and glucose can be used as pharmaceutical agents. Furthermore, Guerrant patent teaches that glutamine derivatives effectively block the degradation of glutamine, and in order to perform effectively in oral therapy, the compounds must be able to survive the conditions in the digestive tract while maintaining the ability to stimulate their absorption and maintain the integrity of the intestinal mucosa. The claims are drawn to "a method of enhancing the absorption of a pharmaceutical agent administered orally to a mammal, comprising the steps of administering to said mammal a composition comprising a glutamine-bearing

compound; and administering orally to said mammal the pharmaceutical agent." The base claim 1 does not recite that the glutamine-bearing compound is not orally administered. Further, the claims do not recite that the glutamine-bearing compound and pharmaceutical agents are administered separately. Therefore, the glutamine-bearing compound and the pharmaceutical agent can be administered at the same time (claim 3), being a conjugated composition, or a pharmaceutical composition (e.g., peptide) can be a glutamine-bearing compound. Furthermore, the reference teaches that modification of amino acid formulation may improve the clinical and metabolic efficacy of parenteral nutrition…glutamine-enriched parenteral or enteral nutrition has been shown to enhance nitrogen balance, attenuate intestinal mucosal damage, decrease bacteremia, and improve survival after irradiation or chemotherapy (see column 2, lines 27-30 and 38-42). The reference teaches that the glutamine-derivative is glutamine coupled with one or more additional amino acids, glucose, glucose and one or more amino acids, or acylating glutamine with a C_2-C_6 carboxylic acids (see column 3, lines 3-12). Again, claim 1 does not define that first step is not administered orally or that the two compounds are separate compounds or in one composition. Furthermore, glutamine-bearing compound can also be a pharmaceutical composition, since any biologically active compounds can be a pharmaceutical composition. Since glutamine-bearing compound of the Guerrant reference is being administered as pharmaceutical composition, and the absorption of a pharmaceutical agent (glutamine) is enhanced, this reference meets the limitation of instant claims. Therefore, the reference anticipates claims 1, 3-7, 9-11, 13-17, and 19.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 11 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Petit et al (US Patent # 6734170).

10. The instant claims are drawn to a method of enhancing the absorption of a pharmaceutical agent administered orally to a mammal, the method comprising the steps of administering to the mammal a composition comprising a glutamine-bearing compound, and administering orally to the mammal the pharmaceutical agent, wherein the mammal is a human subject who is HIV positive, having compromised intestinal function and the administered pharmaceutical agent is an antiretroviral drug.

11. Petit et al teach a composition and a method for increasing cellular uptake of bioactive agents, particularly those compounds termed “small molecules” into the cells of mammalian tissue, such as the epithelial cells of the mucosa (see abstract). The reference teaches that the composition is a solution dispersion or suspension comprising an aqueous vehicle and an effective amount of a bioactive compound, in combination with an amount of carbohydrate effective to reduce the absolute solubility of the bioactive agent in the aqueous vehicle, so as to achieve increased transport (absorption) of the bioactive agent into the target cells (see column 2, lines 35-41). The reference teaches that administration of the composition can provide treatment for a variety of physiologic disorders ameliorated by enhancement of absorption of bioactive agents into damaged or intact tissues (see column 3, lines 5-8). This reads on claim 1 in

part. The reference teaches that the term "bioactive agent" refers to a molecule that exerts a therapeutic or nutritive effect on a mammal following absorption of an effective amount of the molecule by the target (see column 4, lines 9-12). The small molecules that may be potentiated include antiviral drugs and antibiotics (see column 4, lines 55-56) and the specific antiviral agents include acyclovir, acyclovir sodium, amantadine…zidovudine (AZT or ZDY), HPA-23, abacavir (Ziagen®) (see column 5, lines 4-7). This reads on claim 12 in part. The reference further teaches "enhancement of glutamine absorption to treat patients infected with HIV" in column 18. The reference teaches that enhancing glutamine absorption into the intestinal mucosa by the method of administering the composition can provide a therapeutic benefit to HIV-infected patients, particularly those patients who are in the early stages of infection. Enhancement of the cytokine response to the viral infection can contribute to viral destruction by the immune system at the site of significant viral replication (see column 18, lines 30-36). Furthermore, the glutamine/carbohydrate carrier composition can be administered in the form of an enteric-coated tablet, caplet, capsule, or coated bead (see column 18, lines 37-39). This reads on claims 1, 11 and 12.

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 1, 11 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Petit et al (US Patent # 6734170).

13. The instant claims are drawn to a method of enhancing the absorption of a pharmaceutical agent administered orally to a mammal, the method comprising the

steps of administering to the mammal a composition comprising a glutamine-bearing compound, and administering orally to the mammal the pharmaceutical agent, wherein the mammal is a human subject who is HIV positive, having compromised intestinal function and the administered pharmaceutical agent is an antiretroviral drug.

14. Petit et al teach a composition and a method for increasing cellular uptake of bioactive agents, particularly those compounds termed “small molecules” into the cells of mammalian tissue, such as the epithelial cells of the mucosa, as described supra.

Response to Applicant’s Arguments

15. Applicant argues that “the present application teaches and claims using glutamine derivatives to enhance the absorption of other compounds. Petit does not anticipate claims 1, 11 and 12 because it does not anticipate each and every element of the claims, and in fact teaches that the use of carbohydrate to enhance the absorption of compounds such as glutamine." Furthermore, Applicant argues that "the data disclosed in Petit demonstrate and teach the use of various carbohydrates to enhance absorption of various compounds such as glutamine.” Furthermore, Applicant argues that “the cited section merely refers to glutamine acting directly on T cells, not to glutamine enhancing absorption of other compounds.”

16. Applicant’s arguments have been fully considered but have not been found persuasive because the glutamine-carbohydrate conjugate can be considered the pharmaceutical agent. The base claim 1 does not recite that the glutamine-bearing compound is not administered orally. Furthermore, claim 1 does not define that the

glutamine-bearing compound and a pharmaceutical agent are two separate compounds. Thus, any composition comprising a glutamine-bearing compound can be considered a pharmaceutical agent. The carbohydrate is a biologically active agent that can be administered as a pharmaceutical agent. Furthermore, the claims do not disclose that the glutamine-bearing compound and the pharmaceutical agents are administered separately or that these two are two separate compounds. The reference teaches that glutamine-derivatives act to increase the nutritive absorption, thus can be used as a pharmaceutical agent. Since the reference teaches the carbohydrate-glutamine conjugate enhancing the absorption of a "pharmaceutical agent", the reference anticipates the instant claims.

New Objection

17. Claim 19 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 19 is dependent on claim 13. Claim 19 is drawn to "the method of claim 13". Claim 13 is drawn to a composition. Therefore, claim 19 is improperly dependent on claim 13.

18. Claim 22 is objected to because of the following informality: the claim recites, "...drug is selected from the group consisting of zidovudine, lamivudine, stavudine and didanosine, efavirenz, nevirapine and nilfinavir." There appears to be a typographical error. The Examiner believes that the "and" between stavudine and didanosine should

be replaced with a comma, since these two drugs are two different types of reverse transcriptase inhibitors.

19. The specification is objected to due to the following minor informality: at paragraphs [0061] and [0073], there appear to be spelling errors. “HUV positive patients” should be corrected to “HIV positive patients" (for paragraph [0061]) and “HUV infected patients” should be corrected to “HIV infected patients” (for paragraph [0073]).

20. The specification is objected to due to the following minor informality: As described above with the objection to claim 22, the specification recites “stavudine and didanosine” at paragraphs [0038] and [0044]. The errors should be corrected.

New Rejection

35 U.S.C. 112, 2nd

21. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

22. Claims 5 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

23. Claim 5 recites, "the method of claim 3, wherein the glutamine-bearing compound is glutamine, a polymer of glutamine, or a stabilized derivative of glutamine.” The phrase "a stabilized derivative of glutamine" is unclear. It is unclear what type of modifications would be encompassed in the glutamine derivative and what type of glutamine derivatives are stabilized.

24. Claim 14 recites, “the composition of claim 13 wherein the glutamine-bearing compound is glutamine, a polymer of glutamine, or a stabilized derivative of glutamine." The phrase “a stabilized derivative of glutamine” is unclear. It is unclear what type of modifications would be encompassed in the glutamine derivative and what type of glutamine derivatives are stabilized.

35 U.S.C. 112, 1st

25. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9 and 11-17are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.” Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must

describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a pharmaceutical agent and a composition comprising a glutamine-bearing compound. The generic statements a pharmaceutical agent and a composition comprising a glutamine-bearing compound do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1, 5, 7, 9, 13-14, 16-17 are broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that are glutamine-bearing peptides or are in the class of pharmaceutical agents. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may

recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives or variants. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules, other synthetic peptide or peptide-like molecule, any other peptidomimetics or amino mimetics that are glutamine-bearing peptides. Further, the specification is void of organic molecules, small molecules, peptide or peptide-like molecules and any other compounds that are pharmaceutical agents.

The specification discloses that "the term pharmaceutical agent relates to any therapeutic compound that is administered to treat an individual for a disease or malady." The specification discloses that the pharmaceutical agent used in conjunction with the present invention can be any composition that is administered orally for absorption through the small intestine, and in particular include pharmaceuticals that are administered to treat or alleviate the symptoms associated with the condition that caused the intestinal tissue damage…consisting of nutrients, antiviral agents and antibiotics to treat or alleviate symptoms associated with malnutrition, AIDS or tuberculosis (see paragraph [0045]). The specification is limited to the pharmaceutical agent being antiretroviral drugs (ARV). The working examples describe measuring antiretroviral drug levels determination (see Example 3). Example 3 describes the

measurement of zidovudine (AZT) and lamivudine (3TC) or stavudine (D4T) and didanosine (ddI) with either a non-nucleoside reverse transcriptase inhibitor (NNRTI, either efavirenz or nevirapine) or a protease inhibitor (PI, nelfinavir) (see paragraph [0066] for example).The specification discloses that the glutamine composition may comprise glutamine itself, a polymer of glutamine or a stabilized derivative of glutamine (see paragraph [0029]). The specification discloses that the glutamine enriched protein comprises an amino acid sequence selected from the group consisting of (Gln)n, (Ala-Gln)n, (Gln-Y-X)n, (Ala-Gln-Y)n, (Ala-Gln-Y)n, and so on wherein X and Y are independently Gln or Ala, n and p are integers independently 1 to 100, and m is an integer ranging from 1 to 20 (see paragraph [0031]).The specification further discloses that the glutamine-bearing compound is a peptide ranging from 2 to about 20 amino acids in lengths and comprise one or more sequences selected (see paragraph [0032]). The working example describes the Ala-Gln and Gln with all ARV drugs (see paragraph [0067]). The working example only describes Ala-Gln and Gln with antiretroviral drugs, AZT, 3TC, D4T, ddI, efavirenz or nevirapine or nelfinavir (see paragraphs [0060]-[0078] or Example 3). The specification does not describe any other glutamine-bearing compounds or any other pharmaceutical agents other than the anti-retroviral drugs (AZT, 3TC, D4T, ddI, efavirenz or nevirapine or nelfinavir). Description of Ala-Gln and Gln for glutamine-bearing compound and AZT, 3TC, D4T, ddI, efavirenz or nevirapine or nelfinavir is not sufficient to encompass numerous other proteins, peptides, compounds and pharmaceutical agents that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct

qualities that make up the genus. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

35 U.S.C. 102

26. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

27. Claims 1, 3, 5 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller et al (US Patent No. 6,262,019).

28. Keller et al teach nutritional supplement including vitamin C, N-acetyl cysteine (NAC), L-glutamine, whey protein, etc. A high protein, low fat whey has immuno-supportive properties (see column 5, lines 43-44). Vitamin C, NAC, whey protein are all

pharmaceutical agents, meeting the limitation of claims 13-14. The reference teaches that the administration of the dosage units mixed into a liquid 1-4 times a day is useful in the relief of immuno-deficiency in adult humans provoked by infective disease (see column 8, lines 26-30). Furthermore, the reference teaches that the systemic administration of the composition increase energy in people. The reference teaches that the ingredients provide necessary nutrients required for glutathione production while supporting the mammal's ability to produce and preserve existing store GSH (see column 5, lines 47-50), meeting the limitations of claims 1, 3 and 5. Please note: intended use has not been given any patentable weight, since they do not further limit the compound.

29. Claims 13-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Daghfal et al (WO 96/41187).

30. The reference teaches SEQ ID NOS: 1-14 that comprise either Gln or Ala-Gln compounds (see pages 8-9 and SEQ ID NOS: 1-14), meeting the limitation of claims 14, 16-17 and 19. Since the peptides comprise amino acids on either N- or C-terminus of Gln or Ala-Gln compound, this meets the limitation of claim 15. The glutamine compounds (SEQ ID NOS:1-14) and peptide sequences that comprise these glutamines can be considered a pharmaceutical agent, this meets the limitation of claim 13. Please note: intended use has not been given any patentable weight, since they do not further limit the compound.

31. Claims1, 3-5, 7, 11-14, 17 and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Khaled FM (US Patent No. 5,977,073).

32. Khaled patent teaches a composition and method for its use in treatment of an immune disorder in a mammal. The composition includes gamma-L-glutamyl-L-cysteinylglycine, gamma-L-glutamyl-L-cysteine, N-acetyl-L-cysteine (NAC)…L-glutamine, vitamins C, E, β-carotene and vitamin B6 (see abstract and Tables 1-2), meeting the limitations of claims 13-14 and 17. The reference further teaches the disease is preferably treated with some drug therapy, such as AZT, in an amount sufficient to alleviate a symptom of the disease; the causative organism of the infection is HIV, herpes virus, hepatitis virus (see column 3, lines 55-58), meeting the limitations of claims 20-22. Further, the reference teaches that the nutritional composition and methods for use of that composition have been found to significantly enhance the efficacy of treatment of diseases in conjunction with one or more routine drug therapies. The effect is profound and unexpected, in that many symptoms of sever diseases can be significantly alleviated (see column 3, lines 66-67 bridging column 4, lines 1-4). Again, the base claim 1 does not define that the glutamine-bearing compound is not administered orally or at the same as the pharmaceutical agent. The reference teaches the administration of AZT simultaneously with the nutritional composition. The reference teaches the clinical features of patients receiving drug nutrient combination therapy on three human subjects infected with HIV (see Table 3 and column 6, lines 33-38). The reference further teaches that the data indicate that the therapeutic index of the drug nutrient combination therapy is almost ten times higher than that of AZT alone (see

column 5, lines 59-61). Since the reference teaches the enhanced efficacy of drug therapies using the nutritional composition (comprising glutamine), it inherently teaches the enhancing the absorption of the pharmaceutical agent (AZT, in this case), thus meeting the limitations of claims 1, 3-5, 7, 11-12. Please note: intended use has not been given any patentable weight since they do not further limit the compound.

35 U.S.C. 103

33. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

34. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

35. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

36. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Khaled FM (US Patent No. 5,977,073) as applied to claims Claims1, 3-5, 7, 11-14, 17 and 20-22 above.

37. The teachings of Khaled FM patent is described, supra. The difference between the reference and the instant claim is that the reference does not teach the glutamine composition administered prior to the administration of the pharmaceutical agent.

38. However, it would have been obvious to one of ordinary skill in the art to optimize the administration conditions of Khaled patent. Khaled patent teaches that the drug therapy, such as AZT (zidovudine) is treated simultaneously with the nutritional composition (see column 3, lines 55-56, and column 5, lines 19-21). The reference further teaches that with AZT alone, about 75% survival of T-cells was observed compared to control cells; with AZT and the nutritional supplemental such survival was increased to approximately 150%. Thus, the supplement enhances survival of T-cells in the presence of HIV and protects the cells from toxicity of AZT (see column 5, lines 44-57). Thus, it would have been obvious to one of ordinary skill in the art to optimize the administration conditions, since Khaled patent teaches that simultaneous administration

increased the drug efficacy by ten times. One of ordinary skill in the art would have been motivated to optimize, since Khaled patent teaches that with AZT alone, inhibition of growth of normal T-cells is observed, indicating toxicity, and with a combination of AZT and the nutritional supplement, the growth is almost doubled. Since the reference teaches that nutrients increase the health of a patient to which they are administered and the nutrient composition and any standard drug treatment act synergistically to increase the quality of life, and life expectance of a patient (see column 1, lines 57-61). Furthermore, the MPEP states the following: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be

unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). There is a reasonable expectation of success, since administration of nutrient supplement composition with the drug therapy compound simultaneously increased the efficacy of the drug by ten time, thus optimizing the administration conditions would at least optimize the drug absorption efficacy. As described above, it is the normal desire of scientists to improve upon what is already known through routine experimentation. From the teachings of the reference, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention. Thus, the invention as a whole is *prima facie* obvious over the reference, especially in the absence of evidence to the contrary.

Conclusion

39. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. H./
Examiner, Art Unit 1654
/Anish Gupta/

Primary Examiner, Art Unit 1654